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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,479	02/02/2001	Robert L. Bratzler	C1037/7013 (HCL/MAT)	7139

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
08/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/776,479	BRATZLER ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,15-17 and 38-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,15-17 and 38-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment filed April 24, 2008 is acknowledged and has been entered. Claims 1-11, 13, 14 and 18-37 have been canceled. Claim 12 has been amended. Claims 12, 15-17, 38-40, 42, 44, 45, 47, 48 and 52-54 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.

2. This application contains claims 41, 43, 46 and 49-51 are drawn to an invention nonelected with traverse in the paper filed August 18, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 12, 15-17, 38-40, 42, 44, 45, 47, 48 and 52-54 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The pending claims are directed to a method for treating an asthmatic event in a hypo-responsive subject having allergic asthma, comprising: administering to a hypo-responsive subject having allergic asthma a CpG immunostimulatory

nucleic acid (8-100 nucleotides) in an effective amount for treating or preventing an asthmatic event, wherein the hypo-responsive subject is not a neonate. The claims also recite that sub-therapeutic amounts of an asthma/allergy medicament would be administered to the subject.

A review of the specification discloses a list of immunostimulatory nucleic acids that could be used in the claimed method (see Table 1). The specification teaches that "[T]he terms CpG nucleic acid or CpG oligonucleotide as used herein refer to an immunostimulatory CpG nucleic acid or a nucleic acid unless otherwise indicated. The entire immunostimulatory nucleic acid can be unmethylated or portions may be unmethylated but at least the C of the 5' CG 3' must be unmethylated." (specification, p. 34, lines 5-8) However, the instant claims do not recite that the C of the 5'CG3' is unmethylated. The specification discloses method steps/procedures, possible dosages and composition components. However, all of these are described in prophetic terms; there is no enablement/examples set forth in the specification of *in vitro* assays, *in vivo* animal models or *in vivo* human examples that would indicate enablement of the claimed invention.

The state of the art teaches that "[T]he CpG dinucleotides are under-represented and selectively methylated in vertebrate DNA. In contrast, CpG dinucleotides are present at the expected frequency and are unmethylated in bacterial DNA (citation omitted). The recognition of unmethylated CpG dinucleotides within specific flanking bases is believed to be an ancestral nonself pattern recognition mechanism used by the innate immune system to detect DNA of microbes or viruses (citation omitted). In mice, optimal immune activation requires a CpG motif in which an unmethylated CpG dinucleotide is flanked by

two 5' purines and two 3' pyrimidines (3, 4). DNA containing this CpG motif (CpG DNA) activates murine macrophages (5-8), murine dendritic cells (citations omitted), murine NK cells (citations omitted), and murine B cells (citations omitted). CpG DNA is known to be an excellent immune adjuvant in various murine disease models and to drive Thl immune responses (citations omitted). Thus, CpG DNA might be useful for immunotherapy of allergy, infectious disease, and cancer (20, 22-24). The potent adjuvant activity of CpG DNA in mice is most likely based on its stimulatory effects on dendritic cells and B cells. Although CpG effects in mice are well characterized, information regarding the human system is limited." (Hartmann et al, J. Immunology, 2000, 164:944-952, see p. 944 column 1) The state of the art indicates that the 5'CG3' must be unmethylated to achieve this immunostimulatory response.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to practicing the claimed method with an immunostimulatory CpG as presently claimed (i.e. no unmethylated C or unmethylated G, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). With regard to (4) the

nature of the invention and (5) the state of the prior art, these have been discussed above. One of skill in the art would require guidance, in order to make or use the claimed invention of a method for treating an asthmatic event in a hypo-responsive subject having allergic asthma, comprising: administering to a hypo-responsive subject having allergic asthma a CpG immunostimulatory nucleic acid (8-100 nucleotides) in an effective amount for treating or preventing an asthmatic event, wherein the hypo-responsive subject. The recited composition or immuno-stimulatory nucleic acid does not have the same structure that is required according to the state of the art that would possibly have the claimed function.

5. No claims are allowed.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-8975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. M. Minnifield/
Primary Examiner, Art Unit 1645